Amendments to the Claims

Please cancel Claims 1-7, 11-15 and 37. Please amend Claims 8, 16-19, 23, 26-31, 33, 35, and 36. The Claim Listing below will replace all prior versions of the claims in the application:

Claim Listing

1-7 (Cancelled)

8. (Currently Amended) A method for screening a compound that will induce a selective nongenotropic effect of a steroid receptor, comprising:

a) assessing the ability of the compound to activate a ~~pathway~~ nongenotropic activity mediated by the ligand-binding domain of the steroid receptor without substantially activating the DNA-binding domain of the steroid receptor or to activate the DNA-binding domain of the steroid receptor without substantially activating functions mediated by the ligand-binding domain of the steroid receptor; and then

b) measuring the biological activity of the test compound to assess its ability to induce a target nongenotropic effect without substantially inducing a genotropic effect or its ability to induce a target genotropic effect without inducing a substantial nongenotropic effect.

9. (Original) The method of claim 8, wherein the steroid receptor is not the estrogen or progesterone receptor.

10. (Original) The method of claim 8, wherein the steroid receptor is selected from the group comprising a progesterone receptor, a glucocorticoid receptor, a mineralcorticoid receptor, a retinoic acid receptor, vitamin D receptor, PPAR receptor, pregnane X

receptor, bile acid receptor, thyroid receptor, farnesoid X receptor, liver X receptor, ecdysone receptor, and COUP-TF receptor.

11-15 (Cancelled)

16. (Currently Amended) A method for screening a compound to select a compound that induces a ~~selective~~ steroidal response of activating nongenotropic activity and transcriptional activity, comprising:

a) contacting a steroid receptor with a test compound;

b) determining whether a test compound activates the ~~nongentropic~~ nongenotropic activity of a receptor;

c) determining the level of transcriptional activity of the receptor-test compound complex; and

d) selecting the compound that activates the ~~nongentropic~~ nongenotropic activity of the receptor and induces transcriptional activity of the receptor of less than 10% of endogenous steroid receptor ligands.

17. (Currently amended) The method of claim 16, wherein the ~~nongentropic~~ nongenotropic activity is preventing apoptosis.

18. (Currently amended) The method of claim 16, wherein the ~~nongentropic~~ nongenotropic activity is a signal transduction pathway.

19. (Currentl) The method of claim 16, wherein the ~~nongentropic~~ nongenotropic activity is a second messenger system.

20. (Original) The method of claim 18, wherein the signal transduction pathway is a protein kinase signal transduction pathway.

21. (Original) The method of claim 20, wherein the protein kinase signal transduction pathway is a MAP kinase signal transduction pathway.

22. (Original) The method of claim 21, wherein the MAP kinase signal transduction pathway is the Src/Shc/extracellular regulated kinase signal transduction pathways.

23. (Currently Amended) A method of evaluating a compound that induces a nongenotropic effect without substantially inducing a genotropic effect, comprising the steps of:

a) growing a tissue culture cell line until cell growth has reached appropriate confluence;

b) transfecting the tissue culture with an expression plasmid of a specific receptor and an expression plasmid for a target gene responsive to the selected receptor;

c) contacting the transfected cells with a test compound;

d) determining whether the compound induces a nongenotropic effect ;

e) determining whether the compound induces a genotropic effect; and

f) selecting a compound wherein the compound induces a nongenotropic effect without substantially inducing a genotropic effect.

24. (Original) The method of claim 23, wherein the receptor is not an estrogen or progesterone receptor.

25. (Original) The method of claim 23, wherein the target gene is selected from the group consisting of chloramphenicol acetyl transferase (CAT), β-galactosidase, alkaline phosphatase, luciferase, peptide hormones, growth factors and chimeric proteins.

26. (Currently Amended) The method of claim ~~23~~ 25, wherein the level of transcription of the target gene is determined using a method selected from the group consisting of calorimetric, fluorescent; immunochemical, chemical or radiochemical methods.

27. (Currently Amended) A method for screening compounds that activate the nongenotropic activity of the steroid receptor without substantially activating the genotropic activity of the steroid receptor for the treatment of steroid receptor related diseases or disorders comprising:

a) contacting a cell expressing a selected natural or artificial steroid receptor with a test compound;

b) assessing whether the compound activates a ~~nongentropic~~ nongenotropic activity of the steroid receptor;

c) determining the level of transcription induced by the test compound; and

d) selecting the compound or compounds that activate the ~~nongentropic~~ nongenotropic activity of the steroid receptor without substantially activating the genotropic activity of the steroid receptor.

28. (Currently Amended) A method for screening compounds that activate the nongenotropic activity of the steroid receptor without substantially activating the genotropic activity of the steroid receptor for the treatment of steroid receptor related diseases or disorders comprising:

a) contacting a cell expressing a natural or artificial sex steroid receptor with a test compound alone or in combination with a pro-apoptotic agent;

b) assessing whether the compound activates a ~~nongentropic~~ nongenotropic activity of the steroid receptor;

c) determining the level of transcription induced by the test compound;

d) determining whether the test compound inhibited apoptosis in cells contacted with a test compound alone or in combination with a pro-apoptotic agent; and

E) selecting the compound or compounds that activate the ~~nongentropic~~ nongenotropic activity of the steroid receptor without substantially activating the genotropic activity of the steroid receptor.

29. (Currently amended) A method for screening for compounds that modulate the ~~nongentropic~~ nongenotropic activity of a steroid receptor without modulating the genotropic activity of the steroid receptor comprising the steps of:

a) contacting cells expressing a natural or artificial steroid receptor(s) with a test compound;

b) determining the amount of extracellular regulated kinase activation in the cells contacted with the test compound;

c) determining the amount of transcription in the cells contacted with the test compound; and

d) selecting the cells contacted with the test compound that exhibit extracellular regulated kinase activation and minimal transcription levels as compared to transcriptions levels in cells contacted with an androgen or estrogen.

30. (Currently amended) A method for screening for compounds that modulate the ~~nongentropic~~ nongenotropic activity of a steroid receptor without modulating the genotropic activity of the steroid receptor comprising the steps of:

a) contacting cells with at least one test compound wherein the cells contain:

~~(a)~~ (i) non-endogenous DNA which expresses a steroid receptor protein, or functional engineered or modified forms thereof,

~~(b)~~ (ii) DNA which encodes an operative hormone response element

~~(c)~~ (iii) DNA which encodes a second reporter gene operably linked to a signal transduction pathway responsive transcriptional control unit such that transcription of the second reporter gene is activated in response to activating a signal transduction pathway and wherein transcription of the second reporter gene is not

activated by the steroid hormone;

b) assaying for evidence of transcription of the reporter genes in the cells; and

c) selecting the compounds that induce transcription of the second reporter gene and do not induce transcription of the first reporter gene.

31. (Currently amended) A method for screening for compounds that modulate the ~~nongentropic~~ nongenotropic activity of a steroid receptor without modulating the genotropic activity of the steroid receptor comprising the steps of:

a) contacting cells with at least one test compound wherein the cells contain:

~~(a)~~ (i) non-endogenous DNA which expresses a steroid receptor protein, or functional engineered or modified forms thereof,

~~(b)~~ (ii) DNA which encodes a reporter gene operably linked to a signal transduction pathway responsive transcriptional control unit such that transcription of the reporter gene is activated in response to activating a signal transduction pathway and wherein transcription of the second reporter gene is not activated by the steroid hormone;

b) assaying for evidence of transcription of the reporter gene in the cells;

c) quantifying the transcription of steroid receptor responsive genes; and

d) selecting the compounds that induce transcription of the reporter gene and do not induce transcription of steroid receptor responsive genes.

32. (Original) The method of claims 30 or 31, wherein the signal transduction pathway responsive transcriptional control unit is selected from the group consisting of serum response element, Activator protein 1, cAMP response element, E-box DNA binding element, E2F DNA binding element, glucocorticoid response element, heat shock response element, interferon γ activation sequence, interferon stimulated response element, nuclear factor of activated T cells, nuclear factor of κB cells, p53 response element, Rb response element, and STAT3 response element.

33. (Currently amended) A bioassay for identifying a test compound or chemical signal that

activates ~~nongentropic~~ nongenotropic receptor activity without substantially activating genotropic receptor activity, comprising the steps of:

a) growing a tissue culture screening system in a chemically defined culture medium,

b) optionally supplemented with nutrients, wherein the cell line of the tissue culture screening system contains a steroid receptor having at least one identified ~~nongentropic~~ nongenotropic activity;

c) adding a test compound or chemical signal to the medium;

d) measuring the amount of transcription;

e) measuring the amount of ~~nongentropic~~ nongenotropic activity; and

f) selecting the compound that induces ~~nongentropic~~ nongenotropic activity but does not induce transcription.

34. (Original) The method of claim 33, wherein the cell line is OB-6.

35. (Currently amended) A method of screening for ligands of steroid receptors that induce ~~nongentropic~~ nongenotropic activity without substantially inducing genotropic activity is provided comprising the steps of:

a) contacting a cell with a test compound wherein the cell has been transfected with:

i) a DNA sequence encoding a functional steroid receptor or genetic variant of a steroid receptor;

ii) a response element-reporter gene construct; and iii) serum response element-reporter gene construct;

b) determining the effect of the test compound on the transcription of the response element reporter gene construct;

c) determining the effect of the test compound on the transcription of the serum response element-reporter gene construct; and

d) selecting the compound that activates the transcription of the serum response

element-reporter gene construct without substantially effecting the transcription of the

response element reporter gene construct.

36. (Currently Amended) A method of screening for ligands of steroid receptors that induce ~~nongentropic~~ nongenotropic activity without substantially inducing genotropic activity is provided comprising the steps of:

a) contacting a first cell with a test compound wherein the first cell has been transfected with :

i) a DNA sequence encoding a functional steroid receptor or genetic variant of a steroid receptor;

ii) a response element-reporter gene construct;

b) determining the effect of the test compound on the transcription of the response element reporter gene construct;

c) contacting a second cell with the test compound wherein the second cell has been transfected with a signal transduction pathway responsive transcriptional control unit operably linked to a reporter gene;

d) determining the effect of the test compound on the transcription of the second cell; and

e) selecting the compound that activates the transcription of the second cell without substantially effecting the transcription of the first cell.

37. (Cancelled)